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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Michael R. Rosen et al.

Serial No. : 09/898,417

Filed : July 3, 2001

For : A HIGH THROUGHPUT BIOLOGICAL HEART RATE

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1185 Avenue of the Americas New York, New York 10036

October 3, 2002

Assistant Commissioner for Patents Washington, D.C. 20231

SIR:

INFORMATION DISCLOSURE STATEMENT

In compliance with his duty of disclosure under 37 C.F.R. §1.56, applicant directs the Examiner's attention to the following references, which are listed on the accompanying form PTO-1449 (Exhibit 1). Except for reference numbers 4, 7, 20, 23, 27, 37, 41, 49 and 56, which are not readily available all of the information identified on the attached form PTO-1449 is being submitted to the Patent Office in prior application Serial No. 09/875,392 filed June 6, 2001, which is relied upon for a filing date under 35 U.S.C. §120. Therefore, pursuant to 37 C.F.R. §1.198(d) copies of the information identified herein are not

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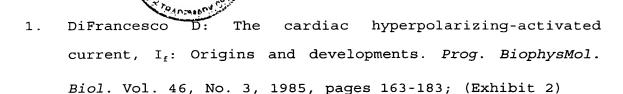
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Filed: July 3, 2001

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required.



- 2. Zhou Z and Lipsius SL: Effect of isoprenaline on I_f current in latent pacemaker cells isolated from cat right atrium: ruptured vs. perforated patch whole-cell recording methods. Pflugers Arch. Vol. 423, No.5 Pt. 6, June 1993, pages 442-447; (Exhibit 3)
- Thuringer D, et al.: A hyperpolarization-activated inward current in human myocardial cells. *JmolCell. Cardiol.* Vol. 24, No. 5, May 1992, pages 451-455; (Exhibit 4)
- 4. Porciatti F, et al.: Block of the pacemaker current I_f in single human atrial myocytes and the effect of beta-adrenoceptor and Al-adenosine receptor stimulation. Br $\it Jpharmacol.$ Vol. 122, No. 6, February 1991, pages 963-969.
- 5. Yu H, et al.: Pacemaker current exists in ventricular myocytes. Circ. Res. Vol. 72, No. 1, January 1993, pages 232-236.; (Exhibit 5)
- 6. Cerbai E, et al.: The properties of the pacemaker current I_f in Human Ventricular Myocytes are modulaed by Cardiac Disease. *Jmol. Cell Cardiol.* Vol. 33, No. 3, March 2001, pages 441-448; (Exhibit 6)

Filed: July 3, 2001

- DiFrancesco D: Generation and control of cardiac pacing: the pacemaker current. Tends Cardiovasc. Med. Vol. 1, 1991, pages 250-255.
- 8. Robinson RB, et al.: Developmental change in the voltage dependence of the pacemaker current, I_f, in rat ventricle cells. *Pflugers Arch.* Vol. 433, 1991, pages 533-535; (Exhibit 7)
- 9. Fares N, et al.: Characterization of a hyperpolarization-activated current in dedifferentiated adult rat ventricular cells in primary culture. J. Physiol. Vol. 506, No. 1, January 1, 1998, pages 73-82; (Exhibit 8)
- 10. Cerbai E, et al.: Influence of postnatal-development on I_f occurrence and properties in neonatal rat ventricular myocytes. Cardiovasc. Res. Vol. 42, No. 2, May 1999, pages 416-423; (Exhibit 9)
- 11. Cerbai E, et al.: Characterization of the hyperpolarization-activated current, I_f, in ventricular myocytes isolated from hypertensive rats. J. Physiol. Vol. 481, No. 3, Dec 15, 1994, pages 585-591; (Exhibit 10)
- 12. Cerbai E, et al.: Characterization of the hyperpolarizationactivated current, I_f, in ventricular myocytes from human failing heart. Circulation. Vol. 95, No. 3, February 4, 1997, pages 568-571; (Exhibit 11)
- 13. Santoro B, et al.: Interactive cloning with the SH3 domain

Filed: July 3, 2001

- of N-src identifies a new brain specific ion channel protein, with homology to Eag and cyclic nucleaotide-gated channels. *Proc. Natl. Sci. USA*. Vol. 94, No. 26, December 23, 1997, pages 14815-14820; (Exhibit 12)
- 14. Ludwig A, et al.: A family of hyperpolarization-activated mammalian cation channels. *Nature*. Vol. 393, No. 6685, June 11, 1998, pages 587-591; (Exhibit 13)
- 15. Santoro B, et al.: Identification of a gene encoding a hyperpolarization-activated pacemaker channel of brain.

 Cell. Vol. 93, No. 5, May 29, 1998, pages 717-729; (Exhibit 14)
- 16. Shi W, et al.: Distribution and Prevalence of hyperpolarization-activated cation channel (HCN) mRNA Expression in Cardiac Tissues. Circ. Res. Vol. 85, No. 1, July 9, 1999, pages el-e6; (Exhibit 15)
- 17. Ishii TM, et al.: Molecular characterization of the hyperpolarization-activated cation channel in rabbit heart sinoatrial node. J. Biol. Chem. Vol. 264, No. 18, April 30, 1999, pages 12835-12839; (Exhibit 16)
- Ludwig A, et al.: Two pacemaker channels from human heart with profoundly different activation kinetics. EMBO J. Vol.
 No. 9, May 4, 1999, pages 2323-2329; (Exhibit 17)
- 19. Moosmang S, et al.: Cellular expression and functional characterization of four hyperpolarization-activated

Filed: July 3, 2001

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pacemaker channels in cardiac and neuronal tissues. Eur. J. Biochem. Vol. 268, No. 6, March 2001, pages 1646-1652; (Exhibit 18)

- 20. Altomare C, et al.: Allosteric voltage-dependent gating of HCN channels. *Biophys. J.* Vol. 80, 2001, pages 241a.
- 21. Protas L, et al.: Chronic neuropeptide Y exposure increases L-type Ca current in neonatal rat cardiomyocytes. Am. J. Physiol. Vol. 277, No. 3 Pt. 2, September 1999, pages H940-H946. (Exhibit 19)
- Kuznetsov V, et al.: β 2-adrenergic receptor actions in neonatal and adult rat ventricular myocytes. Circ. Res. Vol. 76, No. 1, January 1995, pages 40-52; (Exhibit 20)
- 23. Ellingston O, et al.: Adult rat ventricular myocytes cultured in defined medium: phenotype and electromechanical function. Am. J. Physiol. Vol. 265, No. 2 Pt. 2, August 1993, pages H747-H754.
- 24. Ng P, et al.: An enhanced system for construction of adenoviral vectors by the two-plasmid rescue method. Hwn.Gene Ther. Vol. 11, No. 5, March 20, 2000, pages 693-699; (Exhibit 21)
- 25. He TC, et al.: A simplified system for generating recombinant adenoviruses. *Proc. Natl. Acad. Sci. USA*. Vol. 95, No. 5, March 3, 1998, pages 2509-2514; (Exhibit 22)
- 26. Santoro B, et al.: The HCN gene family: molecular basis of

Filed: July 3, 2001

Page 6

the hyperpolarization-activated pacemaker channels. Ann. NY Acad. Sci. Vol.868, April 30, 1999, pages 741-764; (Exhibit 23)

- 27. Accili EA, et al.: Properties and modulation of I_f in newborn versus adult cardiac SA node. Am. J. Physiol. Vol. 272, 1991, pages H1549-H1552.
- 28. Qu J, et al.: Sympathetic innervation alters activation of pacemaker current (I_f) in rat ventricles. J. Physiol. Vol. 526, No. 3, August 1, 2000, pages 561-569; (Exhibit 24)
- 29. Cui J, et al.: Gating of IsK expressed in Xenopus oocytes depends on the amount of mRNA injected. Gen. Physiol. Vol. 104, No. 1, July 1994, pages 87-105; (Exhibit 25)
- 30. Guillemare E, et al.: Effects of the level of mRNA expression on biophysical properties, sensitivity to neurotoxins, and regulation of the brain delayed-rectifier K+ channels Kv1.2. *Biochemistry*. Vol. 31, No. 49, December 15, 1992, pages 12463-12468; (Exhibit 26)
- 31. Honore E, et al.: Different types of K+ channel current are generated by different levels of a single mRNA. EMBO

 J. Vol. 11, No. 7, July 1992, pages 2465-2471; (Exhibit 27)
- 32. Moran O, et al.: Level of expression controls modes of gating of a K+ channel. FEBS Lett. Vol. 302, No. 1, May 4, 1992, pages 21-25; (Exhibit 28)

Filed: July 3, 2001

- 33. DiFrancesco D, et al.: Direct activation of cardiac pacemaker channels by intracellular cyclic AMP. Nature. Vol. 351, No. 6322, May 9, 1991, pages 145-147; (Exhibit 29)
- 34. Kaupp UB, et al.: Molecular diversity of pacemaker ion channels. Annu, Rev. Physiol. Vol. 63, 2001, pages 235-257; (Exhibit 30)
- 35. Chang F, et al.: Effects of protein kinase inhibitors on canine Purkinje fibre pacemaker depolarization and the pacemaker current $I_{\rm f}$. J. Physiol. Vol. 440, 1991, pages 367-384; (Exhibit 31)
- 36. Yu H, et al.: Phosphatase inhibition by calyculin A increases I_f in canine Purkinje fibers and myocytes. Pflugers Arch. Vol. 422, No. 6, March 1993, pages 614-616; (Exhibit 32)
- 37. Accili EA, et al.: Differential control of the hyperpolarization-activated current (I_f) by intracellular cAMP and phosphatase inhibition. *J. Physiol*. Vol. 491, 1996, pages 115.
- 38. Ranjan R, et al.: Mechanism of anode break stimulation in the heart. *Biophys. J.* Vol. 74, No. 4, April 1998, pages 1850-1863; (Exhibit 33)
- 39. Moroni A, et al.: Kinetic and ionic properties of the human HCN2 pacemaker channel. *Pflugers Arch.* Vol. 439, No. 5, March 2000, pages 618-626; (Exhibit 34)

Filed: July 3, 2001

- 40. Santoro B, et al.: Molecular and functional heterogeneity of hyperpolarization-activated pacemaker channels in the mouse CNS. Jneurosci. Vol. 20, No. 14, July 15, 2000, pages 5264-5275; (Exhibit 35)
- 41. Shi W, et al.: The distribution and prevalence of HCN isoforms in the canine heart and their relation to the voltage dependence of $I_{\rm f}$. Biophys. J. Vol. 78, 2000, pages 353A.
- 42. Melman YF, et al.: Structural determinants of KvLQT1 control by the KCNE family of proteins. *J Biol Chem*. Vol. 276, No. 9, March 2, 2001, pages 6439-6444; (Exhibit 36)
- 43. Tinel N, et al.: KCNE2 confers background current characteristics to the cardiac KCNQ1 potassium channel. EMBO

 J. Vol. 19, No. 23, December 1, 2000, pages 6326-6330;

 (Exhibit 37)
- 44. Martens JR, et al.: Differential targeting of Shaker-like potassium channels to lipid rafts. BiolChem. Vol. 275, No. 11, March 17, 2000, pages 7443-7446; (Exhibit 38)
- 45. Chauhan VS, et al.: Abnormal cardiac Na(+) channel properties and QT heart rate adaptation in neonatal ankyrin(B) knockout mice. Circ. Res. Vol. 86, No. 4, March 3, 2000, pages 441-447; (Exhibit 39)
- 46. Walsh KB, et al.: Disctinct voltage-dependent regulation of heart-delayed I_K by protein kinases A and C. Am. J. Physiol.

Filed: July 3, 2001

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Vol. 261, No. 6 Pt. 1, December 1991, pages C1081-C1090; (Exhibit 40)

- 47. Gerhardstein BL, et al.: Proteolytic processing of the C terminus of the alpha (1C) subunit of L-type calcium channels and role of a proline-rich domain in membrane tethering of proteolytic fragments. *J Biol. Chem.* Vol. 275, No. 12, March 24, 2000, pages 8556-8563; (Exhibit 41)
- 48. Barbuti A, et al.: Action of internal pronase on the f-channel kinetics in the rabbit SA node. J. Physiol. Vol. 520, No. 3, November 1, 1999, pages 737-744; (Exhibit 42)
- 49. Wainger BJ, et al.: Domains involved in cyclic nucleotide modulation of hyperpolarization-activated HCN channels.

 Nature. In Press, 2001.
- 50. Wahler GM: Developmental increases in the inwardly rectifying potassium current of rat ventricular myocytes.

 Am. J. Physiol. Vol. 262, No. 5 Pt. 1, May 1992, pages C1266; (Exhibit 43)
- 51. Abbott GW, et al.: MiRP1 forms I_{kr} potassium channels with HERG and is associated with cardiac arrhythmia. *Cell*. Vol. 97, No. 2, April 16, 1999, pages 175-187. (Exhibit 44)
- 52. Sanguinetti MC, et al.: Coassembly of KvLGQT1 and minK (I_{sk}) proteins to form cardiac I_{sk} potassium channels. Nature. Vol. 384, No. 6604, November 7, 1996, pages 80-83; (Exhibit 45)
- 53. Dixon JE and McKinnon D: Quantitative analysis of potassium channel expression in atrial and ventricular muscle of rats.

 Circ. Res. Vol. 75, No. 2, August 1994, pages 252-260;

 (Exhibit 46)

Filed: July 3, 2001

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- 54. Sclagger H and von Jagow G: Tricine-sodium dodecyl sulfate-polyacrylamide gel electrophoresis for separation of proteins in the range from 1 to 100 Kda. *Analytical Biochem*. Vol. 166, No. 2, November 1, 1987, pages 368-379; (Exhibit 47)
- 55. Hansen JE, et al.: Prediction of O-glycosylation of mammalian proteins:Specificity patterns of UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase.

 Biochem. J. Vol. 308, No. 3, June 15, 1995, pages 801-813; (Exhibit 48); and
- 56. Vassalle M, et al.: Pacemaker channels and cardiac automaticity In ''Cardiac Electrophysiology. From Cell to Bedside'', Eds. Zipes D and Jalife WB Saunders Co. Philadelphia, PA, 2000, pages 94-103.

Applicants believe that these references do not anticipate or render obvious applicants' claimed invention. Because this Information Disclosure Statement is being submitted before the mailing of a first Office Action on the merits, no fee is believed to be due. However, in the event that a first Office Action on the merits has been mailed which has not yet reached applicant's attorney, or has not yet been connected to the file in applicant's attorney's office, applicant hereby requests for consideration of this Information Disclosure Statement, pursuant to 37 C.F.R. §1.97(c) and authorize the Office to Charge Deposit

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Account No. 03-3125 the amount of the petition fee in accordance with 37 C.F.R. §1.17(p). In the event that a Notice of Allowance has been mailed, applicant hereby petitions, pursuant to 37 C.F.R. §1.97(d), for consideration of this Information Disclosure Statement, and authorize the Office to charge Deposit Account No. 03-3125 the amount of the fee in accordance with 37 C.F.R. §1.17(i).

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

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